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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,463	02/11/2002	Andrey Rzhetsky	AP34006 070050.1942	4349
21003	7590	04/16/2007	EXAMINER	
BAKER BOTTS L.L.P. 30 ROCKEFELLER PLAZA 44TH FLOOR NEW YORK, NY 10112-4498			DEJONG, ERIC S	
			ART UNIT	PAPER NUMBER
			1631	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		04/16/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/073,463	RZHETSKY ET AL.
	Examiner Eric S. DeJong	Art Unit 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 02 October 2006 and 16 January 2007.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 18, 19, 21, 25-29, 31-33 and 36-45 is/are pending in the application.

4a) Of the above claim(s) 18, 19, 21, 25-29 and 31-33 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 36-45 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 12/04/2006.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_.

## **DETAILED OFFICE ACTION**

### ***Specification***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example paragraph 0032, 0044, and 0056 of the instant specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

### ***Claim Objections***

The objection of claims 36, 38, and 44 is withdrawn in view of amendments made to the instant claims.

### ***Claim Rejections - 35 USC § 112***

The previous rejection of claims 39-42 under 35 USC 112, second paragraph for being indefinite is withdrawn in view of arguments submitted by applicants. Upon further review, it is acknowledged that definitions of the terms recited used equation 5, 6, 14, and 17 are provided in paragraph 0027, 0028, 0060, and, 0062 of the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 recites the limitation "determining attraction probabilities between pairs of molecules of the set of interacting molecules based on known molecular interaction data" in lines 6 and 7 of said claims. Similarly, claim 38 recites "determining probabilities of attraction between conserved features of (interacting) molecules based on known molecular interaction data" in lines 7-9 of said claim. This causes the metes and bounds of the instant claim to be indefinite because it is unclear what the scope and meaning of the recited terms "attraction probabilities" and "probabilities of attraction" actually represent. Neither the claims nor the instant specification set for a clear definition for what an "attraction probability" represents or what features or values from known molecular interaction data are relied upon to determine "attraction probability". For example, paragraph 0028 of the instant specification states:

"(T)he presence of an interaction between proteins is usually backed by multiple experiments while the absence of interaction may correspond to a failed experiment or just the absence of experiments at all (the only exclusion from this observation is exhaustive two-hybrid screening where all results, both positive and negative, are reported). Therefore, the probabilities of "attraction" between two domains should be estimated in such a way that the absence of a connection is treated as the absence of data, while the counts of known connections are used to estimate the probabilities."

While this portion of the specification sets forth that multiple experiments are used to back the presence of interactions between proteins, it does not provide a clear

explanation regarding what experimental data is used in determining probabilities of "attraction" between domains of a protein. It remains unclear if "attraction probabilities" and "probabilities of interaction" as recited in the instant claims is intended to represent an energetic relationship between different domains of interacting molecules or, alternatively, if these terms are intended to represent an abstract correlation between the sequences and/or structures of domains within interacting molecules. If these terms are intended to encompass energetic considerations, it is further unclear how energetic interactions between different domains within interacting molecules, such as bound proteins, can be represented by a statistical "probability".

It is further acknowledged that claim 36, lines 9-11 recites "determining attraction probabilities comprises quantifying the occurrence frequency of said conserved features of said pair of molecules immediately upstream or downstream of each other within known biological system networks". However, it is remains unclear from the instant claim if the recited "conserved features of... known biological system networks" is being used in the context of an actual biological system, as in the case of modeling 3D structure of bound proteins, or, alternatively, if the recited "conserved features of... known biological system networks" is being used in the context of other neural network systems, as in the case of modeling molecular interactions using feed-forward neural networks. Similarly, claim 38 recites "determining probabilities of interaction between conserved features of said molecule and other interacting molecules based on known molecular interaction data of the biological network" in lines 7-9 of said claim. Again, it is unclear from the instant claim if the recited term "biological network" is being used to

describe an actual biological system or, alternatively, some other neural network system. Claims 37 and 39-45 are also included under this rejection due to their dependence from either claim 36 or 38.

Claim 36 further recites the limitation “edge probability” (see lines 12 and 29) of claim 36), which is further defined in the instant claim as being “based on the determined attraction probabilities” (see lines 14-16). In light of the above discussion regarding the indefiniteness of the limitation “attraction probabilities”, the metes and bounds of the limitation “edge probability” are also unclear. Claim 37 is also included under this rejection due to its dependence from claim 36.

Claim 36 further recites the limitations “distribution of edges” (see lines 18 and 19, line 23, and line 25 of said claim) and “edge distribution probability” (see line 22 and line 24 of said claim). This causes the metes and bounds of the instant claim to be indefinite because it is unclear if the recited distribution of edges and edge distribution probability are related to or encompassed by the determined edge probability  $P(E)$ , as set forth in lines 12-16 of the instant claim, or, alternatively, encompass different features of a network topology that are distinct from the determined edge probability  $P(E)$ . If the recited “distribution of edges” and “edge distribution probability” are related to or encompassed by the determined edge probability  $P(E)$ , then, in light of the above discussion regarding the indefiniteness of the limitation “attraction probabilities”, the

metes and bounds of these limitations are also unclear. Claim 37 is also included under this rejection due to its dependence from claim 36.

Claim 36 recites the limitation “determining a posterior probability... using equation 10” in lines 31 and 32 of said claim. This causes the metes and bounds of the instant claim to be indefinite because neither the claim nor the instant specification provide a definition of what a “posterior probability” actually means or encompasses. It is acknowledged that an expression equation 10 is provided in paragraph 0040 of the instant specification, however the terms  $P(\text{network} \mid \text{data})$ ,  $P(\text{network}_i)$ ,  $P(\text{data network}_j)$ , and  $P(\text{network}_j)$  recited in the equation are not defined by either the instant specification nor the instant claims. As such, the meaning and meaning of the term “posterior probability” cannot be determined. Claim 37 is also included under this rejection due to its dependence from claim 36.

Claim 38 recites the limitation “determining probabilities of molecular interactions” which is further defined in the instant claim as being “based on the probabilities of attraction” in lines 10-12 of the instant claim. In light of the above discussion regarding the indefiniteness of the limitation “probabilities of attraction”, the metes and bounds of the limitation “probabilities of molecular interaction” and the means by which this is determined are also unclear. Claims 39-45 are also included under this rejection due to their dependence from claim 38.

Claim 38 recites the limitation “further processor” in line 18 of said claim. This causes the metes and bounds of the claim to be unclear because there is no other “processor” recited in the instant claim. It is acknowledged that the instant claim recites that the method comprises “using a computer to execute instructions” (see line 4 of said claim), however this does not provide an antecedent basis for the limitation of a “further processor”. Claims 39-45 are also included under this rejection due to their dependence from claim 38.

For the purpose of continuing examination, the limitation “further processor” has been construed to read as --another computer--. This rejection could be overcome by amending the instant claim to read as --another computer-- in place of the limitation “further processor”.

***Claim Rejections - 35 USC § 101***

The rejection of claims 38-43 under 35 USC § 101 as being drawn to non-statutory subject matter is withdrawn in view of amendments made to the instant claims.

The rejection of claims 44 and 45 under 35 USC § 101 because the claims lacks patentable utility is withdrawn in view of arguments submitted by applicants.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 36 and 37 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 36 and 37 are drawn to a method for identifying a molecular interaction network representation for a set of interacting molecules within a known biological system. The process for identifying a molecular interaction network representation involves abstract and computational steps for the determination of attraction probabilities, determining an edge probability, determining a network topology, determining a network probability, and identification of a molecular interaction network having the highest posterior probability and, therefore, involves the application of a judicial exception. Regarding inventions involving the application of a judicial exception, said application must be a practical application of the judicial exception that includes either a step of a physical transformation, or produces a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). In the instant claims, there is no step of physical transformation that results from said application of judicial exception, thus the Examiner must determine if said application of a judicial exception produces a useful, concrete, and tangible result.

In determining if the application of a judicial exception produces a useful, concrete, and tangible result, the Examiner must determine each standard individually.

For a result to be “useful,” the application of a judicial exception must produce a result that is specific, and substantial. For a result to be “concrete,” the application of a judicial exception must have a result that is reproducible. For a result to be “tangible,” the application of a judicial exception must produce a real world result . Furthermore, the claim must be limited only to statutory embodiments.

Claims 36 and 37 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application of a judicial exception to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the application of a judicial exception is outputted to a display, a user, a readily accessible memory or other computer on a network, or by including a physical transformation.

### ***Response to Arguments***

Applicant's arguments filed 10/02/2006 and 01/16/2007 have been fully considered but they are not persuasive.

In regards to the withdrawal of claims 18, 19, 21, 25-29, and 31-33 as being drawn to an invention that is independent or distinct from the invention originally claimed, applicants argue that the withdrawn claims are directed to different but similar aspects of the examined claims. Applicants further argue that the withdrawn claims are directed to a method for finding the most likely biological pathway of a set of interacting molecules, which is also the subject matter of claims 36-45.

In response, it is acknowledged that withdrawn claims 18, 19, 21, 25-29, and 31-33 are drawn to a related process to that as recited in instant claims 36-45. Related inventions are distinct if the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; the inventions do not overlap in scope; and the inventions as claimed are not obvious variants. See MPEP § 806.05(j). As set forth in the Office action mailed 06/28/2006, it is reiterated that claims 18, 19, 21, 25-29, and 31-33 are drawn to a method for identifying a most likely biological pathway for a set of interacting molecules comprising the steps of representing a set of interacting molecules as an oriented network graph, assigning a probability to each possible oriented network graph, and selecting an oriented network graph as the most likely biological pathway. As such the invention of claims 18, 19, 21, 25-29, and 31-33 requires the generation and use of oriented network graphs, whereas the originally filed claims and instant claims 36-45 do not. Further, the limitations recited in claims 18, 19, 21, 25-29, and 31-33 for the process steps of representing a set of interacting molecules as an oriented network graph, assigning a probability to each possible oriented network graph, and selecting an oriented network graph as the most likely biological pathway were not recited in the originally presented claims nor are they recited in instant claims 36-45. Therefore, the invention of claims 18, 19, 21, 25-29, and 31-33 has a materially different design, mode of operation, and effect than that of the invention as originally filed and as recited in claims instant claims 36-45. Further, the invention of claims 18, 19, 21, 25-29, and 31-33 is not coextensive in scope

with the invention of claims 36-45 and there is nothing of record to show them to be obvious variants.

In regards to the rejection of claim 36 and 38 under 35 USC § 112, second paragraph for being indefinite, applicants argue that the instant claims have been amended to describe the relationship of “determining attraction probabilities” and “quantifying the occurrence frequency”. Applicants further note that “attraction probabilities” and “probabilities of attraction” are defined in paragraph 0028 of the specification.

In response, it is reiterated from the above rejection that the limitation “determining attraction probabilities between pairs of molecules of the set of interacting molecules based on known molecular interaction data” and recites “determining probabilities of attraction between conserved features of (interacting) molecules based on known molecular interaction data” causes the metes and bounds of the instant claims to be indefinite because it is unclear what the scope and meaning of the recited terms “attraction probabilities” and “probabilities of attraction” actually represent. Applicants arguments and amendments to the instant claims do not address the basis of this rejection for the reasons set forth in the rejection discussed above.

Applicants further argue that paragraph 0023 defines “edge probability” and describe methods for calculating the same, and paragraph 0024 defines “network topology”, “incoming edge”, and “outgoing edge” probability and describes methods for

calculating the same. Applicants further argue Equation 10 of the specification on page 21 provides an explicit Bayesian definition of “posterior probability”.

In response, it is noted that terms recited in the rejected claims are discussed in paragraphs 0020 and 0035 and throughout the disclosure. However, the disclosure does not provide sufficient definitions of the recited claim terminology such the meaning or scope of the instant claims is clear.

In regards to the rejection of claims 36 and 37 under 35 USC § 101 as being drawn to non-statutory subject matter, applicants argue that claim 36 has been amended to include explicit language such that the results are tangibly provided to a use or further processor.

In response, it is noted that claim 38 has been amended to recite that a result is provided to a user or further processor. However, it is noted that instant claim 36 does not contain such an amendment.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shukla Ram can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric S DeJong  
Examiner  
Art Unit 1631

*EDJ*

*John S. Brusca 12 April 2007*  
JOHN S. BRUSCA, PH.D  
PRIMARY EXAMINER